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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/636,530	08/10/2000	Thomas L. Cantor	532212000300	7117

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Peng Chen
Morrison & Foerster
3811 Valley Centre Drive
Suite 500
San Diego, CA 92130-2332

EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/636,530	CANTOR, THOMAS L.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16 and 39-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,16 and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

The request filed on 06 July 2004 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/636,530 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment filed on 06 July 2004 is acknowledged and entered. Following the amendment, claims 22-38 are canceled, and the new claims 39-48 are added.

Currently, claims 14, 16, and 39-48 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 22-38 are moot as the applicant has canceled the claims.

The new matter rejection of claim 14 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's argument.

The rejection of claims 14 and 16 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

The rejection of claims 14 and 16 under 35 U.S.C. 102(b) as being anticipated by Takasu et al. (Endocrinology, 1996, 137(12): 5537-43) is withdrawn in view of applicant's argument.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 48 rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility.

Claim 48 recites that "the PTH antagonist has the further effect of blocking a PTH binding site on a PTH receptor". However, Divieti et al. (Endocrinology, 2002, 143(1):171-176) discloses that human PHT-(7-84) acts via receptors distinct from the PTH1R (the abstract). As

such, the present PTH antagonist, which is the same as that of Divieti's, would not be able to block a PTH binding site on the PTHR as it would not bind PTHR. Therefore, claim 48 is inoperative, and therefore lacks utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The newly added claim 39 is directed to a method for *reducing an anabolic effect* of PTH on bone by administering a PTH antagonist peptide. However, the specification does not teaches why, when or for what condition such reduction of the anabolic effect of PTH would be needed, i.e., what is the use of such a method. Further, the following dependent claims, claims 44-47 for example, recite conditions that can be treated with the claimed method, such as hyperparathroidism, osteodystrophy, osteoporosis and hypercalcemia. However, the common pathological characteristic of these conditions is excess bone resorption due to excess catabolic effect on bone, and/or reduced anabolic metabolism of bone. Therefore, increase in anabolic effect on bone would be needed for these conditions, and they are the direct contraindications for a method for reducing an anabolic effect on bone, such as that of the present invention. Therefore, the presently claimed method is not enabled, and a skilled in the art would not know how to use the claim invention.

Due to the large quantity of experimentation necessary to determine what subject or condition would be suited for a method for *reducing* an anabolic effect of PTH on bone, the lack of direction/guidance presented in the specification regarding same, the complex nature of the invention, the state of the prior art, which has established that increasing an anabolic effect on bone would be needed for conditions such as hyperparathroidism, osteodystrophy, osteoporosis and hypercalcemia, undue experimentation would be required of the skilled artisan to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is indefinite for the limitation of "*a method for reducing an anabolic effect* of PTH on bone in *a subject*" because it is unclear as to who (with what condition) are included by the claim limitation. The metes and bounds of the claim, therefore, cannot be determined.

Claim 47 recites the limitation "*the* further effect" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 48 is similarly indefinite.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

Note: in the prior rejection, the preamble "for reducing an anabolic effect of a PTH on bone" (claim 39) is not given patentable weight as the following method steps, the active ingredient, and diseases being treated are not distinct from that of the prior art.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Born et al. (Endocrinology, 1988, 123(4): 1848-53).

Born discloses a truncated hPHT fragment, hPHT(8-84), which is capable of inhibiting (antagonizing) the biological activity of hPTH (the abstract). Although Born does not explicitly mention a *pharmaceutical* composition of the antagonist of hPTH, it is well known in the art that a purified protein agent is usually used in combination with other agent(s), such as dissolving solutions, and can not be (rather than) used as its crystal form alone. Dissolving solutions, such as water, buffers, or media, would meet the limitation of "pharmaceutical" or "a pharmaceutically acceptable carrier". As such, Born's hPHT(8-84) anticipates claim 14.

Claims 39-42, 44 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukuda, EP 0 528 271 A1.

The teachings of Fukuda were reviewed in the previous Office Actions. Briefly, Fukuda discloses several hPHT muteins, which comprise deletion of 3 to 6 amino acid residues on the N-terminal side of the sequence of hPTH, and teaches that these muteins function as antagonists of hPTH (page 3, lines 12-13). Further, Fukuda teaches that these compounds have more desirable properties in clinical application (page 3, lines 11-15), such as in the treatment of hypercalcemia and the like (page 2, lines 8-9). Although Fukuda does not specifically mention the treatment of hyperparathyroidism with said hPTH antagonist, Fukuda's "the like" would inherently include hyperparathyroidism because it is well established that hyperparathyroidism is due to excess PTH, and Fukuda hPHT muteins are PTH antagonists. As such, the reference anticipates the present claims 39-41, 44 and 47. With respect to the limitation of "with a pharmaceutical carrier or excipient, although Fukuda does not explicitly teach such, it is well known in the art that a purified protein agent is usually used in combination with other agent(s), such as dissolving solutions, and can not be (rather than) used as its crystal form alone. Dissolving solutions, such as water, buffers, or media, would meet the limitation of "a pharmaceutically acceptable carrier or excipient". As such, Fukuda's therapeutic application of the hPTH antagonists to hypercalcemia and the like anticipates claim 42.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Takasu et al. (Endocrinology, 1996, 137(12): 5537-43), and Fukuda, EP 0 528 271 A1.

The teachings of Takasu and Fukuda were reviewed in the previous Office Actions. Briefly, Takasu discloses a truncated hPHT mutein, which N-terminal residue starts at position 35, i.e., hPHT(35-84), and is an antagonist of hPTH as it significantly inhibited the [^{35}S] hPHT(1-84) binding. Fukuda discloses several hPHT muteins, which comprise deletion of 3 to 6 amino acid residues on the N-terminal side of the sequence of hPTH, and teaches that these muteins function as antagonists of hPTH (page 3, lines 12-13). Further, Fukuda teaches that these compounds have more desirable properties in clinical application (page 3, lines 11-15), such as in the treatment of hypercalcemia and the like (page 2, lines 8-9).

Neither reference explicitly teaches a PTH antagonist of PTH_{28-84} or PTH_{34-84}.

However, it would have been obvious to the person of ordinary skill in the art at the time the invention was made that a deletion of the N-terminus of hPTH starting at any position between 3-35 would generate an antagonist of hPTH based on the combination teachings of Takasu and Fukuda; that the minimum size of the fragment as an antagonist of hPTH is hPTH(35-84); and to make such an antagonist such as hPTH(34-84) based on the two references. The person of ordinary skill in the art would have been motivated to do so for treating diseases or conditions such as hypercalcemia as indicated by Fukuda, and reasonably would have expected success because both Takasu and Fukuda have demonstrated that several hPTH fragments, hPTH(3-84), hPTH(4-84), hPTH(5-84), hPTH(6-84), and hPTH(35-84), are hPTH antagonists, and because the hPTH fragments such as those encompassed by the present invention, hPTH(34-84) for example, lack the N-terminal 6 amino acids as Fukuda's, and comprise the minimal fragment of hPTH(35-84) for hPTH antagonists property as defined by Takasu, and therefore,

they fall within the range between hPTH(3-84) and hPTH(35-84), and would be obvious to function as hPTH antagonists.

Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fukuda, EP 0 528 271 A1, as applied to claims 14, 16 and 43 above.

The teachings of Fukuda are reviewed in the previous Office Actions and above. Fukuda does not specifically teach whether the PTH antagonist should be applied in "a pulsatile or a continuous manner".

However, given the current state of the art, determination of an appropriate manner of administering a drug is well within the purview of a person of ordinary skill in the art. Further, most medications can only be given in either a pulsatile or a continuous manner (except a one dose treatment), therefore, such limitations are considered prima facie obvious.

Claims 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fukuda, EP 0 528 271 A1, as applied to claims 14, 16 and 43 above, and further in view of Kanmera et al., EP 0 451 867.

The teachings of Fukuda are reviewed in the previous Office Actions and above. Fukuda does not teach a method for treating renal osteodystrophy or osteoporosis with the hPTH antagonists.

The teachings of Kanmera are reviewed in the previous Office Action, paper No.14, mailed on 26 March 2003, at page 5. Briefly, Kanmera discloses peptide derivatives that are PTH antagonists, and teaches that the derivatives exhibit a potent inhibitory activity against hPTH and are useful as a therapeutic agent for treating dysbolism associated with calcium or phosphoric acid, such as osteoporosis and renal osteodystrophy (the abstract).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the PTH antagonists taught by Fukuda in treating disorders such as osteoporosis and renal osteodystrophy as indicated by Kanmera that PTH antagonists are useful for such disorders. The person of ordinary skill in the art would have been motivated to do so for the treatment of diseases, and reasonably would have expected success because

Kanmera has demonstrated that PTH antagonists are useful as a therapeutic agent in the treatment of osteoporosis and renal osteodystrophy.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
8/16/04